EVALUATION OF CARDIOVASCULAR FUNCTION IN PRIMARY HYPOTHYROIDISM UTILISING ECHOCARDIOGRAPHY

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CERTIFICATE

This is to certify that the dissertation titled "**EVALUATION OF CARDIOVASCULAR FUNCTION IN PRIMARY HYPOTHYROIDISM UTILISING ECHOCARDIOGRAPHY** " is the bonafide original work of DR. M. RAJENDRAN in partial fulfillment of the requirements for M.D. Branch-I (General Medicine) Examination of the Tamilnadu DR. M.G.R Medical University to be held in MARCH 2007. The Period of study was from November 2005 to July 2006.

PROF. S. NATARAJAN, M.D.
Professor and Head of the
Dept. of Medicine,
Govt. Stanley Medical College and Hospital
Chennai-600 001.

DEAN
Govt. Stanley Medical College & Hospital,
Chennai – 600 001.

DECLARATION

I, **DR. M. RAJENDRAN ,** solemnly declare that dissertation titled **"EVALUATION OF CARDIOVASCULAR FUNCTION IN PRIMARY HYPOTHYROIDISM UTILISING ECHOCARDIO GRAPHY"** is a bonafide work done by me at Govt. Stanley Medical College and Hospital during November 2005 to July 2006 under the guidance and supervision of my unit chief **Prof. S. NATARAJAN, M.D.**

This dissertation is submitted to Tamilnadu DR. M.G.R Medical University, towards partial fulfillment of requirement for the award of **M.D. Degree (Branch – I) in General Medicine.**

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Date :

(Dr. M. RAJENDRAN)

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CONTENTS

INTRODUCTION

The thyroid gland maintains the level of metabolism in the tissues that is optimal for their normal function. Thyroid hormones stimulate oxygen consumption of most of the cells in the body, and regulates carbohydrate and lipid metabolism. Thyroid function is regulated by Thyroid stimulating hormone (TSH). Hypothyroidism, a state of deficient thyroid hormones, may be result of many etiologies. Hypothyroidism can affect all organ systems, including cardiovascular system.

The cardiovascular manifestations can be like systolic dysfunction, diastolic dysfunction, pericardial effusion, ECG changes , coronary artery disease and congestive cardiac failure. These dysfunctions can also be contributed by hypertension, hypercholesterolemia which are part of hypothyroidism. Some studies suggest that abdominal aortic atheroscerosis can occur even in mild hypothyroidism.

An understanding of pathophysiology of cardiovascular changes in hypothyroidism enables prevention, early diagnosis and prompt intervention to control complications. Also the presence of cardiovascular complications may necessitate institution of thyroid hormone replacement in patients of asymptomatic hypothyroidism.

This study is undertaken at Stanley Medical College, Chennai to evaluate the cardiovascular changes that accompany various grades of hypothyroidism.

AIM OF THE STUDY

To study the cardiovascular changes in patients with overt primary hypothyroidism utilizing echocardiography.

REVIEW OF LITERATURE

THYROID HORMONES

The principal hormone secreted by the thyroid gland are T4 thyroxine and tri-iodothyronine.T3 is also formed from peripheral deiodination of T4.Both are iodine containing aminoacids.T3 is more active than T4,RT3 is inactive.99.98% of T4 is plasma bound, and biological half life is longer(6-7 days).T3 is less protein bound, so lesser half life. Action of T3 on tissues is more rapid. One third of circulating T4 is normally converted to T3.87% of circulating T3 is formed by deiodination, only 13% of T3 is formed by thyroid gland. Some of the T4 and T3 is further converted into deiodotyrosines.T3 and T4 are also converted into glucuronide conjugates that enter the bile and pass into the intestine. These conjugates will be excreted in stools.T3 acts more rapidly and is 3-5 times more potent than T4.

MECHANISM OF ACTION

Thyroid hormones enter cells, and T3 binds to thyroid receptors (TR) in the nuclei. T4 can also bind, but not as avidly. The hormone-receptor complex then binds to DNA via zinc fingers and increases or in some cases decreases the expression of a variety of different genes that code for enzymes that regulate cell function. Thus, the nuclear receptors for thyroid hormones are members of the super family of hormone sensitive nuclear transcription factors.

There are two human TR genes: an alpha receptor gene on chromosome 17 and a beta receptor gene on chromosome 3. By alternative splicing, each forms at least two different mRNAs and therefore two different receptor proteins. TR beta2 is found only in the brain, but TR alpha 1, TR alpha2, and TR beta1 are widely distributed. TR alpha 2 differs from the other three in that it does not bind T3 and its function is unsettled. TRs bind to DNA as monomers, homodimers, and heterodimers with other nuclear receptors, particularly the retinoid X receptor (RXR). This heterodimer does not bind 9-cis retinoic acid, the usual ligand for RXR, but the TR binding to DNA is greatly enhanced. There are also co activator and co repressor proteins that affect the actions of the TRs. Presumably, this complexity permits thyroid hormones to produce their many different effects in the body, but the overall physiologic significance of the complexity is still largely unknown.

In most of its actions, T3 acts more rapidly and is three to five times more potent than T4. This is because it is less tightly bound to plasma proteins but binds more avidly to thyroid hormone receptors. RT3 is inert.

IODINE METABOLISM

Iodine is a raw material essential for thyroid hormone synthesis. Ingested iodine is converted into iodide and absorbed. The minimum daily iodine intake that will maintain normal thyroid function is 150 micro grams in adults, but in US the average dietary intake is approximately 500 micro gram per day. The

normal plasma iodide level is about 0.3 micro gram per/dl, and iodide is distributed in a space of approximately 25 liter(35% of body weight).The principal organs that take up the iodine are thyroid, which uses it to make thyroid hormones, and the kidneys, which excrete it in the urine.

About 120 micro gram of iodine per day enter thyroid at normal rates of thyroid hormone synthesis and secretion. The thyroid secretes 80 micro grams per day as iodine in T3 and T4. 40 micro grams of iodine per day diffuses into the ECF. The secreted T3 and T4 are metabolized in the liver and other tissues, with the release of 60 micro gram of iodine per day into the ECF.

Some thyroid hormone derivatives are excreted in the bile, and some of the iodine in them is reabsorbed (entero hepatic circulation), but there is a net loss of iodine in the stool of approximately 20 micro gram per day. The total amount of iodine entering the ECF is thus 500+40+60 or 600 micrograms per day. Out of this 600 micrograms of iodine, 20% enters the thyroid gland, whereas 80% is excreted in the urine.

CHEMISTRY AND METABOLISM OF THYROID STIMULATING HORMONE(TSH):

Human TSH is a glycoprotein that contains 211 amino acid residues, plus hexoses, hexosamines and sialic acid. It is made up of 2 sub units, designated as Alpha and Beta. The alpha sub unit is encoded by a gene on chromosome 6 and the beta sub unit by a gene on chromosome 1. The alpha and beta sub units become non covalently linked in the thyrotropes. TSH alpha is identical to the

alpha sub unit of the leutinising hormones, Follicular stimulating hormones and Human Gonodotropic hormone – alpha. The functional specificity of TSH is conferred by the beta sub unit. The structure of the TSH varies from species to species, but other mammalian TSHs are biologically active in humans.

The biologic half life of human TSH is about 60 minutes. TSH is degraded for the most part in the kidneys and to a lesser extent in the liver. Secretion of TSH is pulsatile, and the mean output starts to rise at about 9 pm, peaks at mid night, and then declines during the day. The normal secretion rate is about 110 micro gram per day. The average plasma level is about 2 micro units per ml.

Since the alpha sub unit in the human chorionic gonodotrophin is the same as that in TSH, large amounts of human chorionic gonodotrophin can activate thyroid receptor. In some patients with benign or malignant tumors of placental origin, plasma HCG levels can rise so high that they produce mild hyperthyroidism.

EFFECTS OF TSH ON THE THYROID

When the pitutary is removed, thyroid function is depressed and the gland atrophies; when TSH is administered, thyroid function is stimulated. Within a few minutes after the injection of TSH, there are increases in iodide binding; synthesis of the T3, T4 and iodotyrosines; secretion of thyroglobulin into the colloid; and endocytosis of colloid. Iodide trapping is increased in a few hours;

blood flow increases; and, with chronic TSH treatment, the thyroid cells hypertrophy and the weight of thyroid gland increases.

ACTION OF THYROID HORMONE ON HEART

Heart is a major target organ for thyroid hormone action , and marked changes occur in cardiac function in patients with hypo or hyper thyroidism. Changes can be direct effects of thyroid hormone (T3) or indirect effects. Direct effects results from direct action on heart either by nuclear or extranuclear actions on the cell. Extranuclear effects occur independent of nuclear T3 receptor binding and increases in protein synthesis, influences transport of aminoacids, sugars and calcium across cell membrane.

Nuclear effects are mediated by binding of T3 hormone to specific nuclear receptor proteins. T3 causes increased mRNA coding for sarcoplasmic reticulum ATPase protein, which leads to increase in the speed of diastolic relaxation.

THYROID HORMONE REGULATION OF CARDIAC GENE EXPRESSION

A. Positively regulated :

1. Alpha- myosin heavy chain
2. sarcoplasmic reticulum
3. Ca^{++} - ATPase
4. $Na^{+,}$ k+ ATPase
5. Voltage gated potassium channels

(KV 1.5 , KV 4.2, KV 4.3)

6. Atrial and brain natriuretic peptides
7. Malic enzymes
8. Beta adrenergic receptors
9. Guanine- nucleotide binding protein Gs
10. Adenine nucleotide transporter 1

B. **Negatively regulated** :

1.Beta myosin heavy chain

2. Phospholamban

3.Na+ / Ca++ exchanger

4. Thyroid hormone receptor alpha 1

5. Adenyl cyclase (AC)

6. Guanine nucleotide – binding protein Gi

HEMODYNAMIC ALTERATIONS IN THYROID DISEASE

Predictable changes in myocardial contractility and cardiovascular hemodynamics occur across the entire spectrum of thyroid disease.[1] Multiple studies including those in experimental animals as well as invasive and noninvasive measurements in patients indicate that T3 regulates cardiac inotropy and chronotropy through a variety of direct and indirect mechanisms.

Direct effects on vascular smooth muscle cells decrease systemic vascular resistance of the arterioles of the peripheral circulation.[2] There is a decrease in mean arterial pressure and activation of Renin – Angoitensin –

Aldosterone system which results in an increase in renal sodium reabsorption. This increased sodium reabsorption results in expansion of plasma volume.

The increase in plasma volume coupled with an increase in erythropoietin leads to an increase in blood volume and rise in cardiac preload. So a decrease in the systemic vascular resistance(by as much as 50%) , coupled with increase in venous return and preload, increases cardiac output. Cardiac out put may be more than double in hyperthyroidism and conversely may decrease by as much as 30- 40% in hypothyroidism. Studies using positron emission tomography measurements of acetate metabolism have demonstrated that the marked increase in cardiac output is accomplished with no change in energy efficiency.

T3 appears to reduce systemic vascular resistance by both, direct effects on vascular smooth muscle cells and changes in the vascular endothelium potentially involving the synthesis and secretion of NO.[3] The vasodilatory effect of T3 can be observed within hours of administration of T3 in patients undergoing coronary artery bypass grafting and in patients with chronic congestive cardiac failure. Arterial compliance also falls in hypothyroidism and may explain why mean arterial and diastolic pressure are low and peak systolic pressure increases. Thus the combination of increased cardiac output and decreased compliance, which may be more pronounced in older patients with some degree of arterial vascular disease, leads to systolic hypertension in as many as 30% of patients. One study showed that the prevalence of hypothyroidism in primary pulmonary

hypertension is high.[4] In hypothyroidism, 20% of patients have diastolic hypertension.[5]

EFFECTS OF THYROID HORMONE ON CVS

1. Decreases total peripheral resistance because of cutaneous vasodilatation and this increases sodium and water absorption.
2. By direct action of thyroid hormone on heart, increases cardiac output.
3. By indirect action it increases the sensitivity of heart to catecholamines which causes increase in heart rate, shortening of circulatory time and widening of pulse pressure.

Above effects are caused by increased production of alpha 2 myosin heavy chains, sarcoplasmic reticulum Ca^{++} ATPase, and certain K^{+} channels, and decreased production of beta myosin heavy chains, phospholamban, Na+-Ca+ exchanger

CARDIOVASCULAR CHANGES IN THYROID DISEASE:

Parameter	**Normal**	**Hyperthyroid**	**Hypothyroid**
Systemic vascular resistance (dyne-cm)sec^{-5}	1500 – 1700	700 – 1200	2100 – 2700
Heart rate (beats per minute)	72 – 84	88 – 130	60 – 80
Cardiac output (liter/ minute)	5.8	>7	<4.5
Blood volume (% of normal)	100	105.5	84.5

HYPOTHYROIDISM : Categories

1.Goitrous hypothyroidism

2. Atrophic hypothyroidism

3. Transient hypothyroidism

4. Consumptive hypothyroidism

5. Central hypothyroidism

6. Resistance to thyroid hormone

Primary hypothyroidism accounts for 99% of cases, with 1% account for TSH deficiency, central hypothyroidism. Clinically apparent impairment of thyroid function affects about 2% of adult women and 0.1 to0.2% of adult men.

GOITROUS HYPOTHYROIDISM

Goitrous hypothyroidism can be congenital or acquired. Acquired causes are:

1. Hashimotos thyroiditis

2. Iodine deficiency

3. Drugs

4. Goitrogens

5.Thyroid infiltrations

Atrophic thyroiditis : can be acquired or congenital. Acquired causes are

1. Hashimotos disease

2. Iodide/surgery

SUBCLINICAL HYPOTHYROIDISM

Subclinical hypothyroids, defined by a TSH level above the upper range of the reference population (usually 5 mIU/ML) is seen in as many as 9 percent of unselected populations and prevalence clearly increases with advancing age.[6] In contrast to younger patients, in whom there is a strong female predilection, this difference is lost in older populations. Studies of lipid metabolism, atherosclerosis, cardiac contractility, and systemic vascular resistance are altered in subclinical hypothyroidism. Cholesterol levels rise in parallel with increments in TSH elevations starting at 5 mIU/ml.

In a large study of women in Rotterdam, it was noted that atherosclerosis and myocardial infarction were increased with odds ratios of 1.7 and 2.3 respectively , in women with sub clinical hypothyroidism. Interestingly, the presence of antithyroid antibodies indicated heightened risk.[7] Restoration of serum TSH to normal levels after thyroid hormone replacement therapy, improved lipid levels, lowered systemic vascular resistance, and improved cardiac contractility.[8] In patients with subclinical hypothyroidism, isovolumetric relaxation times are prolonged while systolic contractile function is unchanged. Replacement with L-thyroxin sodium at a mean dose of 68 ug/d (range 50 to 100 ug/d) restored isovolumetric relaxation times to normal, and compared with those in the same patients before therapy, systemic vascular resistance declined and systolic function was significantly improved.[9] A variety of studies have indicated that the changes in systemic vascular resistance may result from alterations in

endothelium-dependent vasodilatation. Taking these findings together, it seems appropriate to recommend thyroid hormone replacement for all patients with subclinical hypothyroidism from a cardiovascular perspective. The lack of untoward cardiac effects observed when serum TSH levels have been restored to normal indicates that the potential benefits far outweigh the risks of treatment.[1]

DIAGNOSIS

Hashimotos disease, radioiodine therapy for Graves disease, and iodine deficiency (in parts of the world where that remains a public health problem) are the leading causes of hypothyroidism and produce diagnostic elevations in serum TSH. Thus, the finding of elevated TSH is sufficient to establish the diagnosis and form the basis for treatment. In routine practice, additional testing with a serum T4 and T3 resin uptake test is confirmatory. The prevalence of hypothyroidism is estimated as 3 to 4 percent for overt disease and 7 to 10 percent for the milder forms of disease. Thus, TSH screening can be advised for all adults and particularly patients demonstrating hypertension, hypercholesterolemia, hypertriglyceridemia, coronary or peripheral vascular disease, unexplained pericardial or pleural effusions, and a variety of musculoskeletal syndromes.[10]

MYXEDEMA COMA

It is the ultimate stage of severe long standing hypothyroidism. This state invariably affects older patients and occurs most commonly during the winter months and associated with a high mortality rate. Usually it is accompanied by

subnormal temperature as low as 23 degree celcius have been reported. The clinical features include the following:

1 . Sinus Bradycardia.

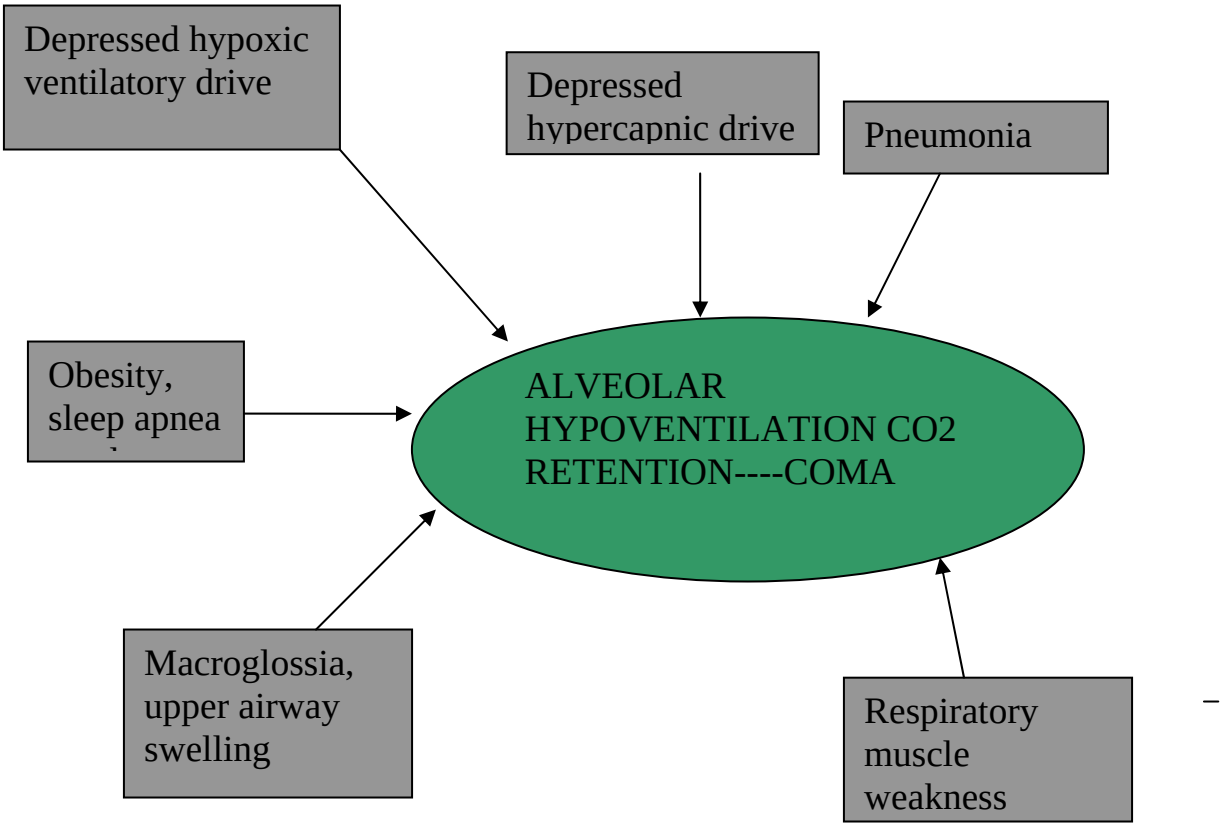
2 . Severe hypotension.

3 . Delay in deep tendon reflexes or areflexia.

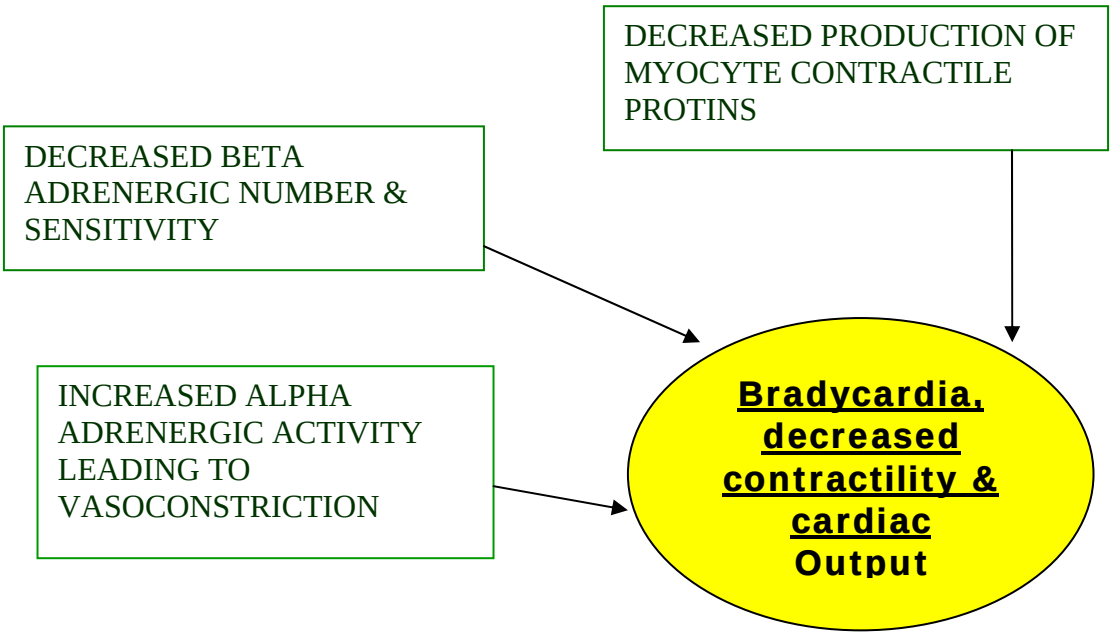
4 . seizures usually accompanying coma.

5 . External manifestations.

PATHOGENESIS OF MYXEDEMA COMA – RESPIRATARY TRIGGERS



PATHOGENESIS OF MYXEDEMA COMA – CARDIOVASCULAR CAUSES



Factors predisposing to myxedema coma are exposure to cold, infection, trauma, CNS depressants, anaesthetics, alveolar hypoventilation and dilutional hyponatremia. There is considerable difficulties in making the diagnosis,because hypothermia due to any cause may produce delayed relaxation of deep tendon reflexes and similarly brain stem infarction in elderly may mimic myxedema coma. Mortality rate of myxedema coma is 20 % or more.[11,12] Hence treatment should be initiated before getting results, on the clinical grounds.

TREATMENT:

It involves hormone replacement and correction of physiological disturbances. Drug administrations should be through intravenous route, because of unpredictable absorption through oral, intramuscular route due to sluggish circulation. The patients are treated with levothyroxine as a single intra venous dose of 500 to 800 microgram. After this daily doses of 100 microgram of levothyroxine are given. Injection hydrocortisone 5 to 10 Mg per hour should also be given because of possibility of adrenocortical hormone deficiency.

Avoid hypotonic fluids, because of water intoxication due to decreased water clearence. Hypertonicfluids may be given to treat dilutional hyponatremia. Respiratory support may be needed in the form of assisted ventilation. Avoid external warming, because it may lead to vascular collapse due to peripheral vasodilatation. Blankets can be used to prevent heat loss. Internal warming should be avoided.

CHANGES IN THYROID HORMONE METABOLISM THAT ACCOMPANY CARDIAC DISEASE

In addition to the changes in thyroid function, which can result from classical, thyroid disease, there are primary alteration in serum total and free T3 and occasionally serum T4 that accompany a variety of acute and chronic illnesses like sepsis, starvation and cardiac disease. In the absence of Thyroid gland abnormality, changes in serum T3 levels result from alterations in thyroid hormone metabolism. These cases have been referred to as “nonthyroidal illness.”

The mechanism for this decrease in serum T3 is multifactorial and in part related to a decrease in 5' mono-deiodination in the liver.

A wide variety of acute and chronic cardiac diseases can alter thyroid hormone metabolism associated with marked declines in serum T3. A population –based study of patients with cardiac disease has shown that a low serum T3 level is a strong predictor of all-cause and cardiovascular mortality.[13] Following uncomplicated acute myocardial infarction, serum T3 levels fall by about 20 percent and reach a nadir after approximately 96 hours. Experimental infarction in animal models produces a similar decrease in serum T3, and replacement of T3 levels to normal has been reported to increase left ventricular contractile function.

Both children and adults undergoing cardiac surgery with cardiopulmonary bypass demonstrate a predictable fall in serum T3 in the preoperative period. Although treatment strategies using acute administration of intravenous T3 to adults after coronary artery bypass grafting have resulted in an improvement in cardiac output and a fall in systemic vascular resistance, there was no alteration in overall mortality. When the prevalence of atrial fibrillation was studied in this group of patients, however, it was shown to be decreased by as much as 50 percent compared with that in age-matched control subjects. Pediatric cardiac patients, especially those undergoing surgery in the neonatal period, demonstrate an even greater decline in serum T3 that can last for longer periods of time. The low postoperative T3 level identifies patients at increased risk for

morbidity and mortality. A prospective randomized study has shown, especially in neonates, that the degree of therapeutic intervention and the need for postoperative inotropic agents are decreased by the administration of T3 in doses sufficient to restore serum T3 levels to normal.

In patients with chronic congestive heart failure, the fall in serum T3 is proportional to the severity of heart failure as assessed by the New York Heart Association classification. As many as 30 percent of patients with heart failure have a low serum T3, which occurs in both patients treated with amiodarone and those who are not. In view of the deleterious effects of hypothyroidism on the myocardium, T3 replacement may be of benefit. Human studies using a novel form of T3 that is capable of restoring serum T3 levels to normal and avoiding the peaks and valleys of drug levels associated with existing drug preparations are required to answer this question.

LIPIDS

Cholesterol is a steroid. It is a precursor to many physiologically important steroids, such as bile acids and steroid hormones. Cholesterol synthesis initially involves the conversion of acetate to mevalonic acid. The rate limiting step is catalysed by the enzyme B – hydroxy methyl glutaryl co-enzyme a reductase (HM GCOA reductase), the activity of which is controlled by negative feedback by the intracellular cholesterol. About 2/3rds of the plasma cholesterol is esterified with fatty acids to form cholesterol esters. Assays in routine use measures the plasma total cholesterol concentrations and do not distinguish between the unesterified and esterified forms. Unlike that of triglyceride, plasma concentration of cholesterol do not rise after a fatty meal.

Lipids are relatively insoluble in water; they are carried in body fluids as soluble protein complexes known as lipoproteins. The core of insoluble (nonpolar) cholesterol esters and triglycerides is surrounded by proteins, phospholipids and free cholesterol with their water-soluble (polar) groups facing outwards.

CLASSIFICATION OF LIPOPROTEINS

Classified according to their density. The greater the lipid/protein ratio in the complex, the larger it is and the lower its density.

THERE ARE 5 MAIN CLASSES OF LIPOPROTEINS

TRIGLYCERIDE – RICH PARTICLES

1. **CHYLOMICRONS** – transport exogenous lipid from intestine to all cells.

2. **VLDL** (Very Low Density Lipoproteins), which transport endogenous lipid from the liver to cells.
3. **IDL** (Intermediate density lipoproteins) usually undetectable in normal plasma. It is normally a transient intermediate lipoprotein formed during the conversion of VLDL to LDL. It contains both cholesterol and endogenous triglycerides.

CHOLESTEROL – RICH PARTICLES

4. **LDL** (Low Density Lipoproteins) formed from VLDL; they transport cholesterol to cells.
5. **HDL** (High Density Lipoproteins) involved in transport of cholesterol from the cells to the liver.

EXOGENOUS LIPID PATHWAYS

Fatty acids and cholesterol, released by digestion of dietary fat together with cholesterol from bile are absorbed into intestinal mucosal cells where they are re-esterified to form triglycerides and cholesterol esters. These together with phospholipids, apo A, apo B are selected from cells into lymphatic system as chylomicrons. This secretion depends on the presence of apo B derived from HDL which are added to them in both lymph and plasma.

LDL is a small cholesterol – rich lipoprotein containing only apoB. It accounts for about 70% of total cholesterol in plasma. It is taken up by specific receptors on cell surfaces (LDL receptors or apo B/E receptors). These receptors are present in all cells, especially abundant in liver. They recognize apo B and apo E and so can take up LDL or IDL. After entering the cells LDL is broken down by lysosomes and the released cholesterol is used up for membrane formation and synthesis of steroid hormones. Cholesterol taken up by receptors, inhibits intracellular cholesterol synthesis and prevents further uptake by reducing the rate of synthesis of LDL receptors. Most of the plasma LDL is removed by LDL receptors. But if plasma concentrations are high some may also enter cells by a passive unregulated route. Due to their small size they can infiltrate tissues such as arterial wall and cause damage.

FACTORS INFLUENCING PLASMA LDL CONCENTRATION

Plasma LDL & therefore plasma cholesterol concentration is determined mainly by rate of uptake of LDL by LDL receptors.

LIVER has central role in cholesterol metabolism because it

- Contains most of the LDL receptors
- Synthesizes most of the endogenous cholesterol
- Receives cholesterol from diet and from lipoproteins
- Is the only organ that can excrete cholesterol from the body in bile.

The concentration of LDL receptors on the hepatic cell surface depends on the amount of cholesterol in the cells. As intracellular cholesterol accumulates, the number of receptors is reduced. Factors that lead to cholesterol accumulation in the liver will, by reducing the receptor numbers, increase plasma LDL concentrations. One of these factors is the amount of cholesterol reaching the liver from the intestine.

Between 30 and 60 percent of cholesterol entering the intestinal lumen from the diet and in the bile is absorbed. The rate of absorption increases if the diet is rich in saturated fat.

Cholesterol may be secreted into plasma, incorporated into VLDL or excreted in bile as cholesterol or bile acids. Some bile acids are reabsorbed from the intestinal lumen and returned to liver via the enterohepatic circulation.

DYSLIPIDEMIA IN HYPOTYROIDISM

Subclinical hypothyroidism results in small increase in LDL cholesterol and a decrease in HDL cholesterol which enhance the risk for developement of atherosclerosis and coronary artery disease. These changes are due to action of thyroid hormone on lipid metabolism. In overt hypothyroidism, increase in total cholesterol, LDL, apolipoprotein B, Lipoprotein A and decrease in HDL occurs, where as in subclinical hypothyroidism increase in total cholesterol and LDL occurs, but no change in HDL or lipoprotein A.[14]

ECG IN HYPOTHYROIDISM

Hypothyroidism tend to produce many ECG changes .The more common manifestations are

1 Sinus bradycardia.

2 . QT prolongation.

3 . Flat or Inverted T waves.

The less common manifestations are :

1 . Heart Block.

2 . Low voltage QRS complexes.

3 . Intraventricular conduction defects.

4 . Ventricular premature depolarizations.

There is decrease in the duration of depolarization in hypothyroidism which results in QT prolongation. Torsades de pointes reported in hypothyroidism is due to QT prolongation, hypothermia, electrolyte disturbances and hypoventilation. Non specific T wave changes are very common, which may be flat or inverted. But ST changes are not usually associated with T wave changes in hypothyroidism, unlike other causes. Duration of repolarization phase of action potential is greatly prolonged in atria of hypothyroidism which accounts for rarity of arrhythmias.[15] Hypothyroidism has a significant antifibrillatory effect on ventricles in dogs.[16]

OBESITY IN HYPOTHYROIDISM

Increased weight gain is a well known feature of hypothyroidism. Because it is a risk factor for coronary artery disease, it is viewed with concern. Morbidly obese patients may present with abnormal thyroid function tests but the reported data are scarce. Marina A et al studied prevalence of hypothyroidism in morbidly obese individuals as 19.5 %.

The reason why obesity occurs in hypothyroidism is due to myxedema. Myxedema is due to accumulation of hyaluronic acid which alters the composition of ground substance in tissues. This is hygroscopic that produces mucinous edema and thickening of skin.

PERICARDIAL EFFUSION

Pericardial effusion may be present in 30% of the patients in hypothyroidism. Pericardial effusion occurs due to increased capillary permeability. Usually pericardial effusion does not compromise cardiac output, and cardiac tamponade is very rare. Usually the pericardial effusion resolves after thyroid hormone replacement.

CORONARY ARTERY DISEASE IN HYPOTHYROIDISM

Because there are many risk factors like hypertension, obesity , hypercholesterolemia and hyperhomocystinemia, hypothyroid patients are prone to coronary artery disease. There is a risk of atherosclerosis and myocardial infarction even in subclinical hypothyroidism.[7]

ECHOCARDIOGRAPHY

Echocardiography is one of the frequently used techniques for diagnosing cardiovascular diseases. It is so versatile, with clinical application in the entire spectrum of cardiovascular diseases. Echocardiography uses high frequency ultrasound to evaluate the structural, functional and homodynamic states of cardiovascular diseases.

An echocardiographic examination begins with trans thoracic two dimensional (2D) scanning from four standard transducer positions: the parasternal, apical, subxiphoid and suprasternal windows. Quantitative measurements of cardiac dimensions, area and volume are derived from 2D

images or 2D derived M-mode. In addition, 2D Echocardiography provides the framework for Doppler and color-flow imaging.

Doppler Echocardiography measures blood-flow velocities in the heart and great vessels and is based on the Doppler Effect. The most common uses of Doppler Echocardiography are pulsed and continuous waveforms. Pulsed wave Doppler is used in determining peak-flow velocity, Valvular pressure gradient, pressure half-time, dynamic left ventricular outflow tract gradient, etc. Colour flow imaging based on Pulsed wave Doppler principles, displays intracavity blood flow in three colors (red, blue, green) or their combinations, depending on the velocity, direction and extent of turbulence. Tissue Doppler provides means for measuring and displaying cardiac wall motion velocities. Tissue Doppler is used to evaluate regional and global diastolic function and it has been noted that mitral annulus velocity measured by Tissue Doppler is an indicator of myocardial relaxation, relatively unaffected by preload or after load.

TREATMENT

The response to treatment of hypothyroidism is predictable, especially from a cardiovascular perspective, Stepwise thyroid hormone replacement using levothyroxine sodium (Levoxyl, Synthroid) produces an incremental decrease in serum TSH, serum cholesterol, and serum CK and an improvement in left ventricular performance. Full replacement is accomplished when serum TSH is normal. In the rare condition of myxedema coma, which is characterized by severe and longstanding hypothyroidism with the development of

hypothermia, altered mental status, hypotension, bradycardia, and hypoventilation, the need for thyroid hormone replacement is more emergent and treatment can be accomplished with either T4 at 100ug/d or T3 25ug/d administered intravenously. These patients often require intensive care unit monitoring with volume repletion, gentle warming, and ventilatory support in the presence of CO2 retention. Administration of hydrocortisone (100 mg every 8 hours) should be undertaken until results of serum cortisol testing are obtained. When patients are treated in this manner, hemodynamics including systemic vascular resistance, cardiac output, and heart rate improve within 24 to 48 hours.

In contrast to overt symptomatic thyroid disease, subclinical thyroid disease implies the absence of classical hyper or hypothyrodism-related symptoms in patients with thyroid dysfunction. The definition has been further refined to include the demonstration of an abnormal TSH level in the presence of normal serum levels of total T4 and free T4. With the advent of widespread TSH screening the magnitude of subclinical thyroid disease may exceed that of overt disease by three to fourfold.

MATERIALS AND METHODS

This study was conducted in patients with hypothyroidism who attended the endocrinology department in Stanley Medical College Hospital, Chennai, during the period November 2005 to July 2006.

1. Patients who were newly diagnosed to have overt hypothyroidism were taken up for the study.

2. Patients thus selected were divided into three categories according to the level of thyroid stimulating hormone (TSH) as follows:

    (i) Mild hypothyroidism (< 20 mIU/ml)

    (ii) Moderate hypothyroidism (20 – 50 mIU/ml)

    (iii) Severe hypothyroidism (> 50 mIU/ml)

3. EXCLUSION CRITERIA - The following patients were excluded from the study:

    - Patients with known primary cardiac disease.
    - Patients with chronic pulmonary disease, severe anemia, diabetes mellitus and chronic kidney disease.
    - Patients who were taking drugs that alter the cardiovascular functions like amiadarone, Beta blockers and calcium channels blockers etc.

- Patients of hypothyroidism who were receiving thyroid replacement therapy.
- Patients with subclinical hypothyroidism (Normal T4 with elevated TSH).

4. All the patients were evaluated for following parameters:
    - Pulse rate
    - Blood pressure - measured thrice and the average was taken (As per recommendations of Joint National Committee – 7)
    - Body mass index (< 25 is normal)
    - Serum free T4 (Normal Range – 4.5 to 12 ng/dl)
    - Serum TSH. (Normal Range – 0.3 to 5.2 mIU / ml)
    - Chest x ray
    - ECG
    - Total cholesterol (As per recommendations of American National Cholesterol Eradication Programe III)

5. Echocardiography was done in all the patients and the following parameters were looked for:
    a) Chamber size and wall thickness : In the 2D and M-mode echocardiography, the measurements of the interventricular septum, left ventricular posterior wall thickness, left ventricular internal diameter

was made in both systole and diastole. Patients with interventricular septal thickness and left posterior wall thickness in diastole more than 1.1 cm represent concentric hypertrophy. Asymmetric hypertrophy is defined as a ratio of interventricular septal thickness and left ventricular posterior wall thickness greater than 1.3. The parasternal long axis view, left ventricular internal diameter in diastole more than 5.6 cm represents dilated left venricle. Left atrial antero posterior diameter more than 3.8cm represents dilated left atrium.

b) Systolic function: The systolic function is assessed mainly by M-mode measurements. Ejection fraction and fractional shortening are the two parameters used. The ejection fraction is defined as the ratio of stroke volume to end diastolic volume.

$$\text{Ejection fraction} = \frac{\text{End diastolic volume - End systolic volume}}{\text{End diastolic volume}} \times 100$$

Normal value of ejection fraction is between 55 to 75%.[17]

Grading of systolic dysfunction:

i) Mild - EF 45 to 55 %

ii) Moderate - EF 35 to 45%

iii) Severe - EF < 35%

Fractional shortening is calculated by the following equation:

$$\text{Fractional shortening} = \frac{LVID(D) - LVID(S)}{LVID(D)} \times 100$$

c. Diastolic function: The diastolic function is assessed by Pulsed wave Doppler using the E/A Measurements. E (m/s)indicate mitral flow which causes ventricular filling following opening of the mitral valve. A (m/s) indicates ventricular filling due to atrial systole. E/A is normally more than 1. Less than 1 indicates diastolic dysfunction.

Diastolic dysfunction can be graded as follows:

Grade 1 = Impaired relaxation

Grade 2 = Pseudonormalised pattern

Grade 3 = Reversible restrictive pattern.

Grade 4 = Irreversible restrictive pattern

d. Left ventricular wall motion abnormalities: Left ventricular performance is assessed by many ways. Left ventricular wall is divided into a number of segments. Determining the motion of each segment provides the wall motion score.

e. Pericardial effusion:The pericardial effusion is quantified by the amount of echo free space surrounding the heart. The pericardial effusion can be graded as :

Minimal pericardial effusion: Posterior atrio-ventricular groove shows echo free space, this is seen in systolic phase only. It represents normal pericardial fluid.

Mild pericardial effusion: Echo free space < 1cm.

Moderate pericardial effusion: Echo free space 1 – 2 cm.

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Large pericardial effusion: Echo free space > 2cm

RESULTS

RESULTS : Total of 40 patients were analyzed and the results were :

TOTAL NUMBER OF PATIENTS - 40

NUMBER OF MALES - 10 (25%)

NUMBER OF FEMALES - 30 (75%)

TABLE - 1

AGE AND SEX DISTRIBUTION

AGE RANGE In YRS	MALE	FEMALE	TOTAL (n-40)
13 – 20	0	04	04 (10%)
21 - 30	02	12	14 (35%)
31- 40	06	09	15(37.5%)
41 - 50	02	05	07 (17.5%)
TOTAL	10(25%)	30(75%)	

MEAN AGE - 32.5 Yrs (RANGE - 13 TO 50 Yrs)

About 72.5% of patients were in the age group of 21 to 40 years of age. 25% were males and 75% were females.

BAR CHART SHOWING AGE DISTRIBUTION

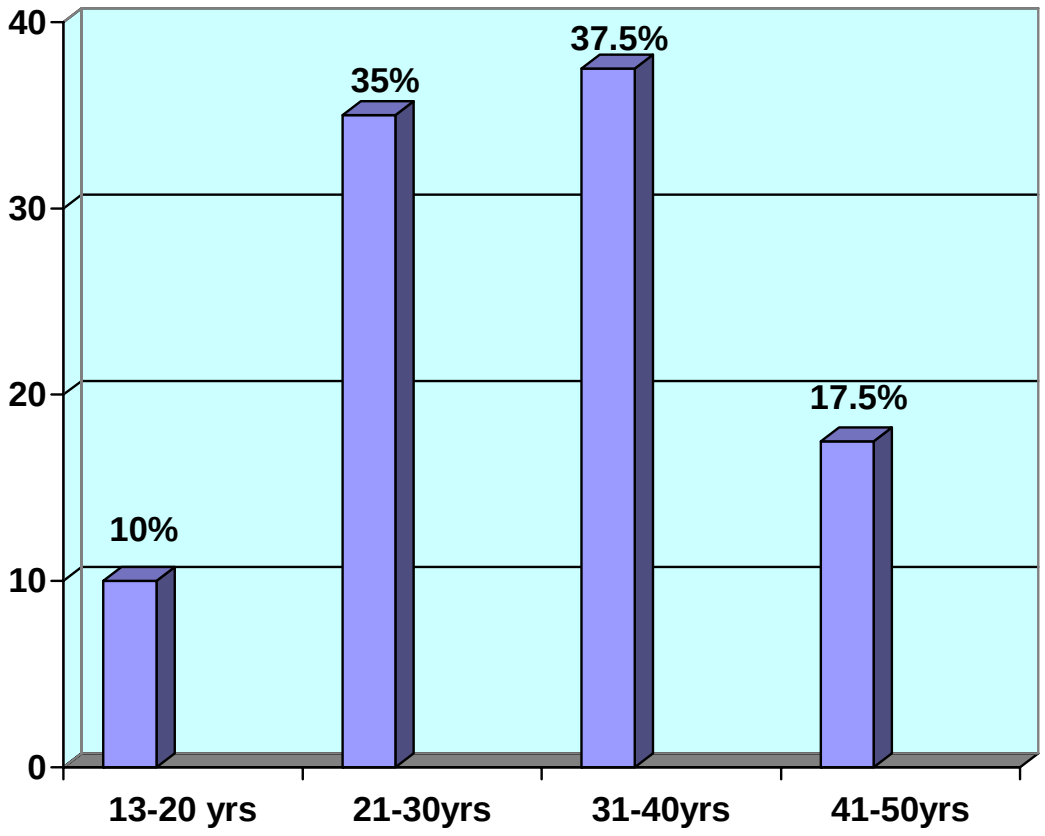

TABLE – 2

SEVERITY OF HYPOTHYROIDISM

GRADING (TSH in mIU/ml)	TOTAL n – 40 (%)
MILD (< 20)	06 (15%)
MODERATE (20 – 50)	17 (42.5%)
SEVERE (> 50)	17 (42.5%)

MEAN - 48.78 mIU/ml (RANGE -9.3 – 135 mIU/ml)

PIE CHART SHOWING GRADING OF HYPOTHYROIDISM

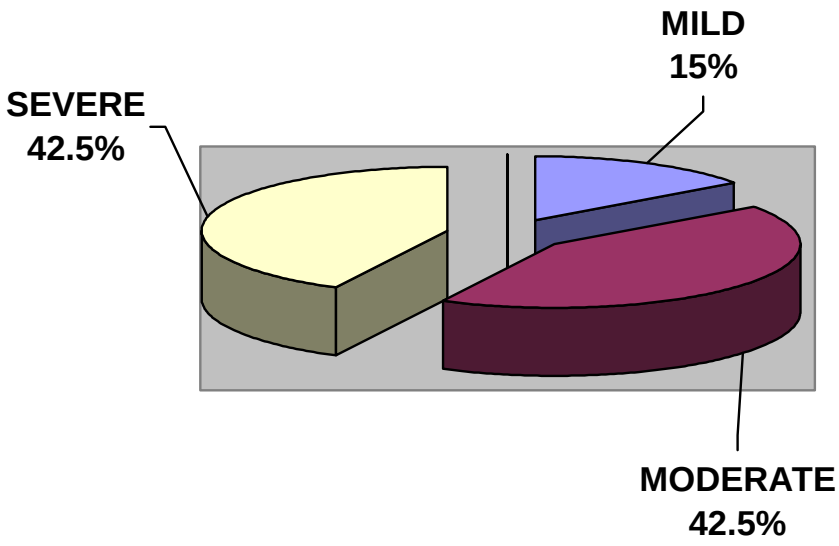

TABLE-3

HYPERTENSION IN HYPOTHYROID PATIENTS

STAGES OF HYPERTENSION (BP in mm Hg)	MALE	FEMALE	TOTAL (n-40)
Pre Hypertension (120 – 139/80-89)	07	09	16 (40%)
Stage – I HTN (140-159/90-99)	03	10	13 (32.5%)
Stage - II HTN (> = 160/100)	0	02	02 (5%)
TOTAL n – 31 (%)	10 (32%)	21 (68%)	

MEAN – 125/82 mmHg (RANGE : 80 – 170/ 60 – 110 mm Hg)

37.5 % of hypothyroid patients were hypertensive (BP >= 140/90 mm Hg)

TABLE - 4

BLOOD PRESSURE AND SEVERITY OF HYPOTHYRODISM

HYPERTENSION	HYPOTHYROIDISM		
	MILD n - 6	MODERATE n - 17	SEVERE n - 17
PRE HTN	02	10	04
STAGE – I	01	01	11
STAGE – II	0	02	0
TOTAL	03 (50%)	13 (76%)	15 (88%)

Hypertension mostly occurred in severe hypothyroidism.

TABLE - 5

ECG CHANGES

ABNORMALITIES	TOTAL n – 40 (%)
Sinus Bradycardia	05 (12.5%)
1st degree AV block	02 (5%)
ST Depression	03 (7.5%)
RBBB	01 (2.5%)

Sinus bradycardia was the most common ECG abnormality noted.

TABLE - 6

TOTAL CHOLESTEROL

Total Cholesterol (mg/dl)	MALE	FEMALE	TOTAL (n-40)
< 200	06	16	22 (55%)
200 – 239	02	09	11 (27.5%)
>= 240	02	05	07 (17.5%)

MEAN CHOLESTEROL – 204.5 mg/dl (Range 143 – 290)

45% of patients had hypercholesterolemia (> = 200 mg/ dl)

TABLE – 7

HYPERCHOLESTEROLEMIA IN HYPOTHYROIDISM

Total Cholesterol (mg/dl)	HYPOTHYROIDISM		
	MILD n - 6	MODERATE n - 17	SEVERE n - 17
200 – 239	01	04	06
>= 240	0	0	07
TOTAL (n- 18)	O1 (5.5%)	04 (22.2%)	13 (72.2%)

72.2% of hypercholesterolemia occurred in severe form of hypothyroidism

TABLE - 8

BODY MASS INDEX

BODY MASS INDEX	HYPOTHYROIDISM			TOTAL n-40 (%)
	MILD n - 6	MODERATE n - 17	SEVERE n - 17	
< 25	05	08	06	19 (47%)
25 – 30	0	09	07	16 (40%)
> 30	01	0	04	05 (12.5%)

Gross obesity occurred only in 12.5% of hypothyroid patients.

TABLE - 9

SEPTAL WALL THICKNESS

SEPTAL THICKNESS	HYPOTHYROIDISM			TOTAL n-40 (%)
	MILD n - 6	MODERATE n - 17	SEVERE n - 17	
< 9 mm	0	03	0	03 (7.5%)
9 – 11 mm	05	07	05	17 (42.5%)
> 11mm	01	07	12	20 (50%)

MEAN – 11mm (RANGE – 7 – 14 mm)

Septal hypertrophy occurred in 50% of the patients.

TABLE – 10

LEFT VENTRICULAR POSTERIOR WALL THICKNESS

POSTERIOR WALL THICKNESS	HYPOTHYROIDISM			TOTAL n-40 (%)
	MILD n - 6	MODERATE n - 17	SEVERE n - 17	
< 9 mm	02	06	0	08 (20%)
9 – 11 mm	04	08	06	18 (45%)
> 11mm	0	03	11	14 (35%)

MEAN – 10mm (RANGE – 6 – 13 mm)

Left ventricular posterior wall hypertrophy occurred in 35% of patients

TABLE – 11

LEFT VENTRICULAR EJECTION FRACTION IN HYPOTHYROIDISM

EJECTION FRACTION (%)	HYPOTHYROIDISM			TOTAL n-40 (%)
	MILD n - 6	MODERATE n - 17	SEVERE n - 17	
< 55%	0	0	01	01 (2.5%)
55 – 60 %	0	03	09	12 (30%)
> 60 %	06	14	07	27 (67.5%)

MEAN – 63.3% (RANGE – 52 – 73%)

Most of the hypothyroid patients had normal left ventricular ejection fraction.

TABLE – 12

FRACTIONAL SHORTENING IN HYPOTHYROIDISM

FRACTIONAL SHORTENING (%)	HYPOTHYROIDISM			TOTAL n-40 (%)
	MILD n - 6	MODERATE n - 17	SEVERE n - 17	
< 28%	0	0	0	0
28 – 35 %	0	12	14	26 (65%)
> 35 %	06	05	03	14 (35%)

MEAN – 33.5% (RANGE – 28 – 41%)

Fractional shortening is normal in all the patients

TABLE – 13

DIASTOLIC DYSFUNCTION IN HYPOTHYROIDISM

E / A RATIO	HYPOTHYROIDISM			TOTAL n-40 (%)
	MILD n - 6	MODERATE n - 17	SEVERE n - 17	
< 1	01	03	09	13 (32.5%)
1– 1.5	02	09	07	18 (45%)
> 1.5	03	05	01	09 (22.5%)

MEAN – 1.2 (RANGE – 0.7 to 2.7)

32.5% of patients had significant diastolic dysfunction

TABLE – 14

LEFT VENTRICULAR INTERNAL DIMENSION IN HYPOTHYROIDISM

LV ID (D) IN cm	HYPOTHYROIDISM			TOTAL n-40 (%)
	MILD n - 6	MODERATE n - 17	SEVERE n - 17	
< 4cm	01	0	02	03 (7.5%)
4– 5cm	05	15	08	28 (70%)
> 5 cm	0	02	07	09 (22.5%)

MEAN – 4.6cm (RANGE – 3.4 – 5.2 cm)

None of the patients had dilated left ventricle.

TABLE – 15

SEPTAL WALL THICKNESS AND BLOOD PRESSURE

IVST	AND BLOOD PRESSURE		
	PRE HTN	STAGE - I	STAGE - II
>11mm	06	12	02
PERCENTAGE n - 20	30%	60%	10%

70% of patients with septal wall thickness had hypertension (BP > = 140/90)

TABLE – 16

HYPERTENSION & DIASTOLIC DYSFUNCTION

DIASTOLIC DYSFUNCTION	PRE HTN	STAGE – I HTN	STAGE – II HTN	NORMAL BP
E/A < 1 (n – 13)	02 (15.4%)	09 (69%)	01 (7.6%)	01 (7.6%)

77 % of hypothyroid patients with diastolic dysfunction had hypertension.

TABLE – 17

AGE AND WALL THICKNESS

AGE IN YEARS	MEAN IVST (D) cm	MEAN LVPW (D) cm
13 – 20	0.82	0.77
21 - 30	1.14	1.02
31- 40	1.07	1.01
41 - 50	1.26	1.15

The mean wall thickness increases with increasing age.

DISCUSSION

Thyroid hormone exerts various actions on cardiovascular system. In hypothyroid state, the decreased myocardial contractility and increased peripheral vascular resistance along with bradycardia produces many changes in the heart. This study is undertaken to assess the cardiovascular changes in overt newly diagnosed primary hypothyroid patients attending endocrine department at Stanley Medical college hospital.

A total of 40 newly diagnosed hypothyroid Patients were analyzed. There were 30 (75%) females and 10 (25%) males. The mean age of presentation was 32.5Years.The age range noted was between 13 to 50 years.73% of patients were in the age group of 21 to 40 Years of age. The mean age for males was 35 Years and for females 31 Years. Most of the females 21 (70%) belonged to 21 to 40 Years. Most common age group studied was 31 to 40 Years (37.5%).

Of the 40 patients studied, 6 (15%) patients had TSH values of less than 20, classified as mild hypothyroidism. Moderate hypothyroidism (TSH 20-50) and Severe Hypothyroidism (TSH more than 50) were present in 17 (42.5%) patients each. Mean TSH value was 48.8 IU/L and the range of TSH noted was between 9.3 and 135 IU/L.

15 (37.5%) patients had hypertension of which 13(32.5%) had stage I and 2(5%) stage II hypertension. 9(22.5%) had normal blood pressure. 16 (40%) had pre hypertension of which,7 were males and 9 females. Out of 15 patients of hypertension, 12 (80%) were females and 3 (20%) were males. The mean systolic

Blood Pressure was 125mm Hg and mean diastolic Blood Pressure was 82 mm Hg. The range of Systolic Blood Pressure noted was between 80 to 170mm Hg and diastolic Blood Pressure ranged from 60 to 110mm Hg. Biondi et al reported a mean systolic Blood Pressure of 120mm Hg and mean diastolic pressure of 78mm Hg.[9] DH Streeten et al study observed a prevalence of 3.6% of hypothyroidism in a population of obesity.[18]

Among 31 cases of hypertension, 16 (51.6%) had prehypertension, 13 (41.9%) patients had stage 1 hypertension and 2 (6.4%) patients had stage II hypertension. The incidence of hypertension in mild, moderate and severe hypothyroidism was 1 (16.6%), 3 (17.6%) and 11 (64%) in respective categories. There was no stage II hypertension in mild and moderate hypothyroidism. In our study it has been found that hypertension commonly occurs with increasing severity of hypothyroidism (TSH levels). Bergus et al reported no correlation between hypertension and TSH levels.[19,20] Danzi S et al reported a 20 % diastolic hypertension in hypothyroidism.[5]

16 (40%) patients were overweight (BMI 25-30), 5(12.5%) were obese (BMI > 30) and 19 (47%) patients had normal body mass index. Out of 16 overweight patients, 7 (43.7%) had severe hypothyroidism and 9 (56.2%) had moderate hypothyroidism. Out of 5 obese patients, 4 (80%) had severe hypothyroidismand 1 (20%) had mild hypothyroidism. The mean body mass index noted was 25.7. The mean body mass index noted in mild, moderate and severe hypothyroidism were 23.8, 24.8 and 27.2 respectively. In our study it was

observed that mean BMI increases with increasing levels of TSH. Marina A et al observed an incidence of 11% of hypothyroidism in obese individuals.[21]

Various ECG abnormalities have been noted in patients with hypothyroidism in our study. Most common abnormality was sinus bradycardia, which was noted in 5(12%) patients. Other ECG abnormalities noted were ST depression in 3 (7.5%) patients and 1st Degree heart block in 2 (5%). Only one patient had Right Bundle Branch Block .No patient had low voltage QRS complex or QT prolongation.

Hypercholesterolemia (> 200 mg/dl) was noted in 18 (45%) patients of which 11 (27.5%) had serum cholesterol between 200- 239 and 7 (17.5%) had Cholesterol level more than 240. 22 (55%) patients had normal cholesterol level. The mean cholesterol level noted was 204.5 mg / dl. The range of cholesterol level was from 143 to 290 mg / dl. Out of 18 patients with hypercholesterolemia 13 had severe hypothyroidism, 4 had moderate and 1 had mild hypothyroidism. 76% of severely hypothyroid patients had serum cholesterol more than 200 mg/dl.

The mean cholesterol level in mild, moderate and severe hypothyroidism were 174.3 mg /dl,191 mg / dl and 229 mg / dl respectively. Cholesterol level above 240 was present in only in severe hypothyroid patients. In our study the cholesterol level increases with increasing levels of TSH. Kung et al reported an incidence of 50% of hyperlipoprotinemia in subclinical hypothyroidism.[22]

ECHOCARDIOGRAPHIC PROFILE

INTERVENTRICULAR SEPTAL WALL THICKNESS:

Most common abnormality noted in echocardiography is septal wall thickness. 50% of patients had increased septal wall hypertrophy. Septal wall thickness more than 11 mm was noted in 20(50%) patients, between 9-11mm in 17(42.5%) patients and less than 9mm in 3(7.5%) patients. The mean septal wall thickness was 11mm. The mean septal wall thickness in mild, moderate and severe hypothyroidism was 10 mm, 10 mm and 11 mm respectively. The range of septal wall thickness was from 7 mm to 14 mm. Out of 20 patients who had septal wall hypertrophy 12 had severe hypothyroidism , 7 had moderate and one had mild hypothyroidism. 70% of severe hypothyroid and 42.5% of moderately hypothyroid patients had septal wall hypertrophy. In our study there is a steady increase in septal wall thickness with increasing severity of hypothyroidism. Varma et al had reported a mean septal wall thickness of 0.91 cm in moderate and 0.97 cm in severe hypothyroidism patients.[23]

Biondi et al reported a mean septal wall thickness of 0.98 cm in subclinical hypothyroid patients.[9] Rawat et al reported a mean septal wall thickness 1.2 cm in hypothyroid patients.[24]

LEFT VENTRICULAR POSTERIOR WALL THICKNESS:

14 (35%) patients had Left ventricular posterior wall thickness of more than 11mm, 18(45%) patients had 9-11mm and 8(20%) patients had less than 9mm thickness. Out of 14 patients who showed Left ventricular posterior

wall hypertrophy, 11 (78.5%) had severe hypothyroidism, 3 (21.5%) had moderate hypothyroidism and none of the mild hypothyroid patient showed Left ventricular posterior wall hypertrophy. 65% of severely hypothyroid and 17% of moderately hypothyroid patients had left ventricular posterior wall hypertrophy.

Mean Left ventricular posterior wall thickness was 1.018 cm. The mean Left ventricular posterior wall thickness in mild, moderate and severe hypothyroidism noted were 0.88 cm, 0.98 cm and 1.09 cm respectively. The ratio of septal hypertrophy and Left ventricular posterior wall thickness more than 1.3 is termed as Asymmetric hypertrophy. In our study the ratio of septal hypertrophy and Left ventricular posterior wall thickness was less than 1.3. So there was symmetrical hypertrophy of septal and Left ventricular posterior wall. Rawat et al, Biondi et al and Varma et al noted a mean Left ventricular posterior wall thickness of 1.1 cm., 0.89 cm and 1.3 cm respectively in their study of hypothyroid patients.[24,9,23]

SYSTOLIC DYSFUNCTION:

Most of the patients (97.5%) of patients had Ejection Fraction more than 55%, of which 12(30%) patients had ejection fraction between 55 – 60% and 27 (67.5%) patients had ejection fraction of more than 60%. Only one patient (2.5%) had ejection fraction less than 55% ,who was severely hypothyroid. The mean ejection fraction was 63.3%. The mean ejection fraction in mild, moderate and severe hypothyroidism was 69%, 63.5% and 61%. These observations led to a

conclusion that systolic function was less affected in hypothyroidism. The mean ejection fraction of left ventricle noted in Rawat et al study was 59%.[24]

Among 40 patients of hypothyroidism none of the patients had fractional shortening of less than 28%. Fractional Shortening between 28 to 35% and more than 35% was noted in 26(65%) and 14(35%) patients respectively. The mean Fractional Shortening was 33.5% ranging between 28 – 41 %. The mean Fractional Shortening in mild, moderate and severe hypothyroidism noted were 39.17%, 34.29% and 33.12% respectively. Fractional Shortening is not significantly affected in hypothyroidism in the present study. Biondi et al and Rawat et al noted a mean Fractional Shortening of 37% and 27.3% respectively in their study of hypothyroid patients.[9,24] Grossman et al (1994) and Varma et al (1995) did not find any evidence of systolic dysfunction in hypothyroid patients.[25,23]

DIASTOLIC DYSFUNCTION:

13 (32.5%) patients had a E/A ratio of less than 1, 18(45%) had between 1 to 1.5 and 9(22.5%) had more than 1.5. Out of 13 patients who showed diastolic dysfunction (E/A ratio < 1) 9 were severely hypothyroid and 3 were moderately hypothyroid. 53% of severely hypothyroid patients and 18% of moderately hypothyroid patients had diastolic dysfunction. The mean E/A ratio was 1.2. The range of E/A ratio varied from 0.7 to 2.7. The mean E/A ratio observed in Bernadette Biondi et al study was 1.3 cm in sub clinical

hypothyroidism.[9] Varma et al from safdarjang Hospital New Delhi observed diastolic dysfunction in significant number of patients in overt hypothyroidism.[23] Diastolic dysfunction is second most common abnormality after septal and posterior wall thickness in hypothyroidism.

LEFT VENTRICULAR DILATATION:

3 (7.5%) patients had left ventricle internal dimension in diastole of less than 4 cm, 28 (70%) had left ventricle internal dimension in diastole of 4 - 5 cm, and 9 (22.5%) had left ventricle internal dimension in diastole of more than 5 cm. But none of the patients had more than 5.5 cm. of left ventricle internal dimension in diastole, which indicates left ventricular enlargement. The mean left ventricular internal dimension was 4.7 cm and the range was from 3.4 cm to 5.2 cm. Rawat et al noted the mean left ventricle internal dimension in diastole of 5.5 cm.[24] Biondi et al noted a mean left ventricle internal dimension in diastole of 4.7 cm.[9] To conclude left ventricle internal dimension in diastole has no changes in the present study as what was observed in varma R et al study.[23]

PERICARDIAL EFFUSION:

Pericardial effusion was found in 3 (7.5%) cases. Of these 3 patients, 2 of them were moderately hypothyroid and 1 had severe hypothyroidism. All the 3 patients with Pericardial effusion had only mild Pericardial effusion, which is defined as an echo space of less than 1 cm. Hardisty

et al studied 39 patients and observed Pericardial effusion in 12 (30.7%) patients, who were severely hypothyroid.[26] Kabadi et al noted Pericardial effusion only in 3 and 6% in mild and severe hypothyroidism respectively.[27] But Rawat et al observed Pericardial effusion in 72% of patients with hypothyroidism but no pericardial effusion in patients less than 30 years.[24] Varma et al reported Pericardial effusion only in overt hypothyroidism.[23] Fouron et al pointed out low incidence of pericardial effusion in young patients.[28]

AGE AND WALL THICKNESS:

Literature shows that there are increased incidence of asymmetric or concentric wall thickness in hypothyroid patients but latter it was pointed out that most of the patients were relatively older, and most of them might have age related wall thickening. Studies done by Bennet et al, Lee et al, and Bernstein et al did not find significant wall thickness in young individuals.[29,30,31]

In our study, the mean septal wall thickness noted in the age groups 13-20 yrs, 21-30, 31- 40 and 41-50 were 0.82 cm, 1.14cm , 1.07cm and 1.26cm respectively.The mean left ventricular posterior wall thickness noted in the age groups 13-20 yrs, 21-30, 31- 40 and 41-50 were 0.77 cm,1.02cm, 1.01cm and 1.1cm respectively. These observations make it clear that there is increase in mean septal wall thickness with increasing age, as what was suggested by Rawat et al.[24]

Among these 20 patients with Septal hypertrophy, Pre Hypertension was present in 6 (30%) patients and the remaining 14 (70%) had Hypertension. Out of 13(32.5%) patients with diastolic dysfunction,10 (77%) had hypertension, 2 (15.4%) had Pre Hypertension and 1 (7.6%) had normal Blood Pressure.

This study highlighted the role of echocardiography in assessing the cardiovascular changes that occur in hypothyroidism. The most common abnormality observed was septal and LV posterior wall hypertrophy. Diastolic dysfunction was noted in significant number of patients. There was no systolic dysfunction or left ventricular dilatation.

SUMMARY

1. A total of 40 patients were analyzed. There were 30 females and 10 males. Mean age of presentation was 32.5 years.
2. There were 15 % Mild hypothyroidism,42.5% Moderate hypothyroidism and 42.5 % Severe hypothyroidism patients.
3. 40% of patients were overweight and 12.5 % of patients were obese.
4. Hypercholesterolemia occurred in 45 % and Hypertension occurred in 37.5 %.
5. Chest xray was normal in all patients.
6. Commonest ECG abnormality noted was sinus bradycardia .
7. In echocardiographic study, interventricular septal wall and left ventricular posterior wall hypertrophy noted in 50 % and 35 % of patients respectively.
8. Diastolic dysfunction was observed in 32.5 % (E/A ratio < 1)
9. Grade 1 systolic dysfunction was noted only in one patient(2.5 %).
10. Pericardial effusion occurred in 3 patients (7.5 %).
11. Dilated left ventricle / left atrium or regional wall motion abnormalities were not found in any patient.

CONCLUSION

- Echocardiography is easily performed, noninvasive, safe, reproducible and accurate in assessment of cardiac function in hypothyroidism.

- Hypertrophy of interventricular septum and left ventricular posterior wall was the commonest abnormality observed in echocardiography.

- Diastolic dysfunction occurred in significant number of hypothyroid patients.

- The cardiovascular changes were more marked in severe hypothyroidism.

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PROFORMA

Name : **Age:** **Sex:**

TSH LEVEL

T 4 LEVEL

Clinical Features:

- **HEIGHT**
- **WEIGHT**
- **BMI**
- **PULSE RATE**
- **BLOOD PRESSURE**

Laboratory profile

- **ECG**
- **CHEST X RAY**
- **SERUM TOTAL CHOLESTEROL**
- **ECHOCARDIOGRAPHY –** **Septal wall thickness**

  Posterior wall thickness

  Fractional shortening

  Ejection fraction

  Diastolic dysfunction (E/A ratio)

  LVID

  Pericardial effusion

  RWMA